



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

[Handwritten mark]

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|----------------------|---------------------------|------------------|
| 10/018,770 | 12/17/2001 | Yoshihito Ikeda | F-7178 | 2012 |
| 277 | 7590 | 07/08/2005 | EXAMINER | |
| PRICE HENEVELD COOPER DEWITT & LITTON, LLP | | | PRATS, FRANCISCO CHANDLER | |
| 695 KENMOOR, S.E. | | | | |
| P O BOX 2567 | | | ART UNIT | PAPER NUMBER |
| GRAND RAPIDS, MI 49501 | | | 1651 | |

DATE MAILED: 07/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | |
|---|------------------------|---------------------|
| Advisory Action Before the Filing of an Appeal Brief | Application No. | Applicant(s) |
| | 10/018,770 | IKEDA ET AL. |
| | Examiner | Art Unit |
| | Francisco C. Prats | 1651 |

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 29 June 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
 - a) The period for reply expires 3 months from the mailing date of the final rejection.
 - b) The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
 - (a) They raise new issues that would require further consideration and/or search (see NOTE below);
 - (b) They raise the issue of new matter (see NOTE below);
 - (c) They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
 - (d) They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. Applicant's reply has overcome the following rejection(s): _____.
6. Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

7. For purposes of appeal, the proposed amendment(s): a) will not be entered, or b) will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____

Claim(s) objected to: _____

Claim(s) rejected: 1,4,6-8,10-14 and 19.

Claim(s) withdrawn from consideration: _____

AFFIDAVIT OR OTHER EVIDENCE

8. The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. The request for reconsideration has been considered but does NOT place the application in condition for allowance because: see attachment.
12. Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. Other: _____

ATTACHMENT TO ADVISORY ACTION

The response filed June 29, 2005, has been received and entered. The entire record of this application has been thoroughly reviewed. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

All of applicant's argument has been fully considered but is not persuasive of error. Applicant refers to "inaccurate statements and conclusions set forth in the Advisory Action dated June 21, 2005." Response of June 29, 2005, page 1. It is unclear how a description of the references' disclosures can be inaccurate. If anything, applicant's characterization of the references is incomplete, and ignores statements that undermine applicant's position. If anything, applicant fails to recognize the entire disclosures of the references, particularly JP '882, as well as the state of the art in general, thereby failing to consider the prior art as a whole. It is unequivocal that an obviousness analysis under § 103(a) requires assessment of the prior art as a whole, in its entirety. See, e.g., MPEP § 2141.02, subsection entitled "**PRIOR ART MUST BE CONSIDERED IN ITS ENTIRETY, INCLUDING DISCLOSURES THAT TEACH AWAY FROM THE CLAIMS**" (emphasis added); citing, *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983),

Art Unit: 1651

cert. denied, 469 U.S. 851 (1984). Applicant's analysis fails this test.

For example, applicant states that "[n]one of the prior art references teach or suggest that either human PC-SOD or human SOD undergo denaturation during a freeze-drying process."

Response of June 29, 2005, page 2. It is applicant's statement which is not accurate. JP '882 clearly states, with respect to underivatized SOD, that "even with the combination of aldose monosaccharides such as galactose, arabinose, glucose, and the like to human SOD prior to freeze-drying, **analysis by anion-exchange chromatography reveals denaturation** (Comparative Example 3)." JP '882, translation, page 4, emphasis added. Applicant's argument entirely ignores this statement in JP '882, and entirely ignores the Comparative Examples in JP '882 which demonstrate denaturation of SOD.

It is true, as argued by applicant, that JP '279 does not describe any stability problem with respect to PC-SOD. However, it is a scientific fact that the protein portion of PC-SOD is subject to degradation by proteases, and one of ordinary skill would recognize this. The fact that the protein portion of PC-SOD is subject to protein degradation is evidenced by JP '882, which, again, clearly states that with respect to underivatized SOD, that "even with the combination of aldose monosaccharides

Art Unit: 1651

such as galactose, arabinose, glucose, and the like to human SOD prior to freeze-drying, **analysis by anion-exchange chromatography reveals denaturation** (Comparative Example 3)."

JP '882, translation, page 4, emphasis added. Given the fact that the protein portions of PC-SOD and SOD are identical, one of ordinary skill, absent evidence to the contrary, would expect at least somewhat similar behavior between the two compounds.

At the very least applicant has failed to provide any direct evidence to the contrary. Thus, as stated in the previous office action, the artisan of ordinary skill, recognizing from JP '882 that addition of sucrose to the freeze-drying mixture of SOD avoids the denaturation problems accompanying the SOD freeze drying process, clearly would have been motivated to have added sucrose to the freeze-drying mixture of the PC-SOD of JP '279, so as to avoid any denaturation of the PC-SOD. Recognizing that the protein portion of the PC-SOD of JP '279 was the same as the protein portion of the SOD of JP '882, the artisan of ordinary skill would have reasonably expected the freeze drying process of JP '882 to have been applicable to the freeze drying process of JP '279. The rejection of record must therefore be maintained.

It is noted that JP '882, as quoted in the response of June 29, 2005, states that "[n]o decrease in the enzymatic action of

Art Unit: 1651

human SOD is observed when this protein is subjected to freezing and thawing or freeze-drying processes, nor is formation of insoluble matter visible to the naked eye." JP '882, translation, page 3. However, as discussed above, JP '882 also states unequivocally that SOD denaturation is recognizable by other means (e.g., chromatography) and is a problem which should be avoided when SOD is applied in freeze-drying storage applications. Thus, for the same reasons, one of ordinary skill would have expected denaturation to have been a problem when storing PC-SOD, as has been discussed at length on the record, and as stated at length above.

Applicant again asserts, at great length, that the stability problem with SOD is not present with PC-SOD, alluding to the supposed different mechanisms of degradation of SOD and PC-SOD, including the "large steric hindrance" by the phosphatidylcholine moieties appended to the SOD protein in PC-SOD, as well as the fact that the dimerization that occurs with SOD does not occur with PC-SOD. However, applicant's argument lacks evidentiary support, and therefore cannot properly be used as a basis to overcome the *prima facie* holding of obviousness. See MPEP § 2145, stating that

The arguments of counsel cannot take the place of evidence in the record. *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); *In re Geisler*, 116

Art Unit: 1651

F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997) ("An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a *prima facie* case of obviousness.").

To date, the only direct evidence presented to date regarding the degradation of PC-SOD is the Rule 132 Declaration of Yoshitoma Morizawa of December 23, 2004. That Declaration demonstrates only that, at certain temperatures, storage of PC-SOD over a number of days results in a lowering of pH due to release of palmitic acid. The Declaration demonstrates nothing about how and whether the protein portions of the PC-SOD and SOD molecules are degraded differently, how the phosphatidylcholine moiety affects that degradation, and whether the artisan of ordinary skill would have ignored what is plainly demonstrated by the cited references.

As to applicant's supposed solution of a different problem, it is well established that claimed subject matter is properly considered obvious under § 103(a) as long as the prior art suggests practicing the claimed subject matter, even if the prior art's reason for practicing the claimed subject matter is different than applicant's. See, e.g., MPEP § 2144, subsection entitled "RATIONALE DIFFERENT FROM APPLICANT'S IS PERMISSIBLE" and cases cited therein. Moreover, it does not truly appear that a different problem is being solved, since a known

Art Unit: 1651

stabilizing agent, sucrose, is being used for a purpose identical to which it was put in the past -- stabilization of a preparation having superoxide dismutase activity. Moreover, the use of sucrose cannot be considered unexpected, as argued, since it is one of the stabilizing agents explicitly named by the JP '882 reference.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Francisco C. Prats whose telephone number is 571-272-0921. The examiner can normally be reached on Monday through Friday, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Art Unit: 1651

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).



Francisco C. Prats
Primary Examiner
Art Unit 1651

FCP